AMENDMENTS TO THE CLAIMS

The following listing of the claims replaces all prior claims presented in the application:

1. (Currently amended) A method of treating neuromuscular dysfunction of the lower urinary tract in a mammal in need of such ~~treat ment~~ treatment comprising administering to said mammal an effective amount of a compound having selective affinity for the mGlu5 subtype of the metabotropic glutamate receptors.

2. (Currently amended) The method of claim 1 wherein said compound has an at least about 10-fold ~~slectivity~~ selectivity for the mGlu5 subtype of the metabotropic glutamate receptors.

3. (Original) The method of claim 1 wherein said compound has an at least about 25-fold slectivity for the mGlu5 subtype of the metabotropic glutamate receptors.

4. (Original) The method of claim 1 wherein said compound has an at least about 50-fold slectivity for the mGlu5 subtype of the metabotropic glutamate receptors.

5. (Original) The method of claim 1 wherein said compound has an at least about 100-fold slectivity for the mGlu5 subtype of the metabotropic glutamate receptors.

6. (Original) The method of claim 1 wherein said compound has an at least about 500-fold slectivity for the mGlu5 subtype of the metabotropic glutamate receptors.

7. (Original) The method of claim 1 wherein said compound is a selective mGlu5 receptor antagonist.

8. (Original) The method of claim 7 wherein said neuromuscular dysfunction is urinary urgency, overactive bladder, increased urinary frequency, decreased urinary compliance, cystitis,

incontinence, urine leakage, enuresis, dysuria, urinary hesitancy or difficulty in emptying the bladder.

9. (Original) The method of claim 8 wherein said neuromuscular dysfunction that is decreased urinary compliance is decreased bladder storage capacity.

10. (Currently amended) The method of claim 8 wherein said ~~said~~ neuromuscular dysfunction is interstitial cystitis.

11. (Original) The method of claim 1 wherein said compound is administered as a pharmaceutically acceptable composition.

12. (Original) The method of claim 11 wherein said compound is administered via an oral, parenteral, intranasal, sublingual, rectal or inhalatory route, or by insufflation, transdermal patches or lyophilized composition.

13. (Original) The method of claims 1 wherein said compound is administered in an amount of between about 0.01 to about 25 mg/kg/day.

14. (Original) The method of claim 13 wherein said compound is administered in an amount of between about 0.1 to about 10 mg/kg/day.

15. (Original) The method of claim 14 wherein said compound is administered in an amount of about 0.2 to about 5 mg/kg/day.

16. (Original) The method of claim 1 wherein said compound is administered at a total daily dose of about 25 to about 1000 mg.

17. (Original) The method of claim 16 wherein said compound is administered at a total daily dose of about 150 to about 500 mg.

18. (Original) The method of claim 17 wherein said compound is administered at a total daily dose of about 350 mg.

19. (Original) The method of claim 1 wherein said compound is administered in combination with an antimuscarinic drug.

20. (Original) The method of claim 19 wherein said antimuscarinic drug is selected from the group consisting of oxybutynin, tolterodine, darifenacin and temiverine.

21. (Original) The method of claim 1 wherein said compound is administered in combination with an α1-adrenergic antagonist.

22. (Original) The method of claim 21 wherein said α1-adrenergic antagonist is selected from the group consisting of prazosin, doxazosin, terazosin, alfuzosin and tamsulosin.

23. (Original) The method of claim 1 wherein said compound is administered in combination with a 5-HT_{1A} receptor antagonist.

24. (Original) The method of claim 1 wherein said compound is administered in combination with a selective COX2 inhibitor.

25. (Original) The method of claim 24 wherein said selective COX2 inhibitor comprises a NO releasing group.

26. (Original) The method of claim 1 wherein said compound is administered in combination with a non-selective COX1/COX2 inhibitor.

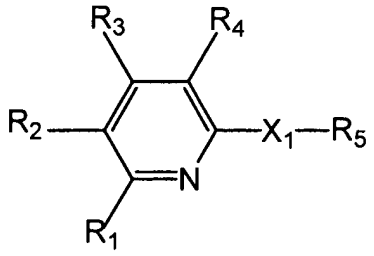
27. (Original) The method of claim 26 wherein said non-selective COX1/COX2 inhibitor derivative comprises a NO releasing group.

28. (Original) The method of claim 1 wherein said mammal is a human.

29. (Original) The method of claim 1 wherein said compound is administered in admixture with a pharmaceutically acceptable diluent or carrier.

30. (Original) The method of claim 29 wherein said pharmaceutically acceptable diluent or carrier is selected from the group consisting of ethanol, water, glycerol, aloe vera gel, allantoin, glycerine, vitamin A oil, vitamin E oil, mineral oil, phosphate buffered saline, PPG2 myristyl propionate, magnesium carbonate, potassium phosphate, vegetable oil, animal oil, and solketal.

31. (Currently amended) The method of claim 1 wherein said compound having selective affinity for the mGlu5 subtype of the metabotropic glutamate receptors has a general formula I



(I)

wherein:

R_1 represents hydrogen, lower alkyl, lower hydroxyalkyl, lower alkylamino, piperidino, carboxyl, esterified carboxyl, amidated carboxyl, lower alkoxy, lower haloalkyl, lower haloalkoxy, cyano, alkynyl, lower alkoxycarbonyl, di-(lower)alkylamino, lower alkylaminocarbonyl, trifluoromethylphenylaminocarbonyl or N-(lower)alkyl-N-phenylcarbamoyl, said N-(lower)alkyl and N-phenyl radicals being unsubstituted or substituted independently with a substituent selected from the group consisting of lower alkyl, lower alkoxy, halogen, and trifluoromethyl groups,

R_2 represents hydrogen, lower alkyl, carboxyl, esterified carboxyl, amidated carboxyl, lower hydroxyalkyl, hydroxyl, lower alkoxy or lower alkanoyloxy, lower alkoxycarbonyl, di-

(lower)-alkylamino-(lower)alkanoyl, di-(lower)alkylaminomethyl, 4-(4-fluorobenzoyl)-piperidin-1-yl-carbonyl, 4-*tert*-butyloxycarbonylpiperazin-1-yl-carbonyl, 4-(4-azido-2-hydroxybenzoyl)-piperazin-1-yl-carbonyl or 4-(4-azido-2-hydroxy-3-iodo-benzoyl)-piperazin-1-yl-carbonyl,

R_3 represents hydrogen, lower alkyl, carboxy, lower alkoxycarbonyl, lower alkylcarbamoyl, lower hydroxyalkyl, di-(lower)alkylaminomethyl, morpholinocarbonyl or 4-(4-fluorobenzoyl)piperidin-1-yl-carbonyl,

R_4 represents hydrogen, lower alkyl, hydroxyl, lower hydroxyalkyl, lower aminoalkyl, (lower)alkylamino(lower)alkyl, di-(lower)-alkylamino(lower)alkyl, unsubstituted or hydroxy-substituted (lower)alkyleneamino(lower)alkyl, lower alkoxy, lower alkanoyloxy, lower aminoalkoxy, (lower)alkylamino(lower)alkoxy, di-(lower)-alkylamino(lower)alkoxy, lower alkoxycarbonyl, carboxy(lower)alkylcarbonyl, (lower)alkoxycarbonyl(lower)alkoxy, lower hydroxyalkyl, m-hydroxy-p-azidophenylcarbonylamino(lower)alkoxy, lower aminoalkoxy, phthalimido(lower)alkoxy, unsubstituted (lower)alkyleneamino(lower)alkoxy or (lower)alkyleneamino(lower)alkoxy ~~substitued~~ substituted with hydroxyl or 2-oxo-imidazolidin-1-yl-groups, carboxyl, esterified carboxyl, amidated carboxyl, lower carboxyalkoxy or lower esterified carboxyalkoxy,

X_1 represents a lower alkenylene, lower haloalkenylene, lower alkynylene or lower haloalkynylene group, wherein each of the foregoing groups is linked via vicinal unsaturated carbon atoms, or an azo group (-N=N-), and

R_5 represents an aromatic or heteroaromatic group which is unsubstituted or substituted with one or more substituents selected from lower hydroxyalkyl, lower alkoxycarbonyl, lower alkanoyl, trifluoromethyl, trifluoromethoxy, trimethylsilylalkynyl, azido, lower aminoalkoxy, di-(lower)-alkylamino(lower)alkoxy, monohalobenzylamino, thienylmethylamino, thienylcarbonylamino, trifluoromethylphenylaminocarbonyl, tetrazolyl, lower alkanoylamino, benzylcarbonylamino, (lower)alkylaminocarbonylamino, (lower)alkoxycarbonylaminocarbonylamino, (lower)alkylsulfonyl, lower alkyl, halo, lower haloalkyl, lower haloalkoxy, lower alkenyl, lower alkynyl, unsubstituted phenyl or phenyl substituted with one or more substituent selected from the group consisting of lower alkyl, lower alkoxy, halo and trifluoromethyl groups, unsubstituted phenyl(lower)alkynyl or

phenyl(lower)alkynyl substituted with one or more substituent selected from the group consisting of lower alkyl, lower alkoxy, halo and trifluoromethyl groups, hydroxyl, lower hydroxyalkyl, (lower)alkanoyloxy(lower)alkyl, lower alkoxy, lower alkenyloxy, lower alkylenedioxy, lower alkanoyloxy, lower amin alkoxy, (lower)alkylamino(lower)alkoxy, (lower)alkanoylamino(lower)alkoxy, N-(lower)-alkyl-N-(lower)-alkanoylamino(lower)alkoxy, unsubstituted phenoxy or phenoxy substituted with one or more substituent selected from the group consisting of lower alkyl, lower alkoxy, halo and trifluoromethyl groups, phenyl(lower)alkoxy or phenyl(lower)alkoxy wherein the phenyl group is substituted with one or more substituent selected from the group consisting of lower alkyl, lower alkoxy, halo and trifluoromethyl groups, acyl, carboxyl, esterified carboxyl, amidated carboxyl, cyano, carboxy(lower)alkylamino, esterified carboxy(lower)alkylamino, amidated carboxy(lower)alkylamino, phosphono(lower)alkylamino, esterified phosphono(lower)alkylamino, nitro, amino, lower alkylamino, di-(lower)-alkylamino, acylamino, N-acyl-N-(lower)-alkylamino, phenylamino, phenyl(lower)alkylamino, cycloalkyl(lower)alkylamino or heteroaryl(lower)alkylamino each of which may be unsubstituted or lower alkyl- lower alkoxy-, halo- and/or trifluoromethyl-substituted,

or an enantiomer, diastereoisomer, N-oxide, crystalline form, hydrate, solvate, pharmacologically active metabolite, prodrug, or pharmaceutically acceptable salt thereof.

32. (Original) The method of claim 31 wherein said compound has a structure wherein

X_1 is a (C_{2-4})alkenylene, (C_{2-4})haloalkenylene, (C_{2-4})alkynylene or (C_{2-4})haloalkynylene group, wherein each of the foregoing groups is bonded via vicinal unsaturated carbon atoms;

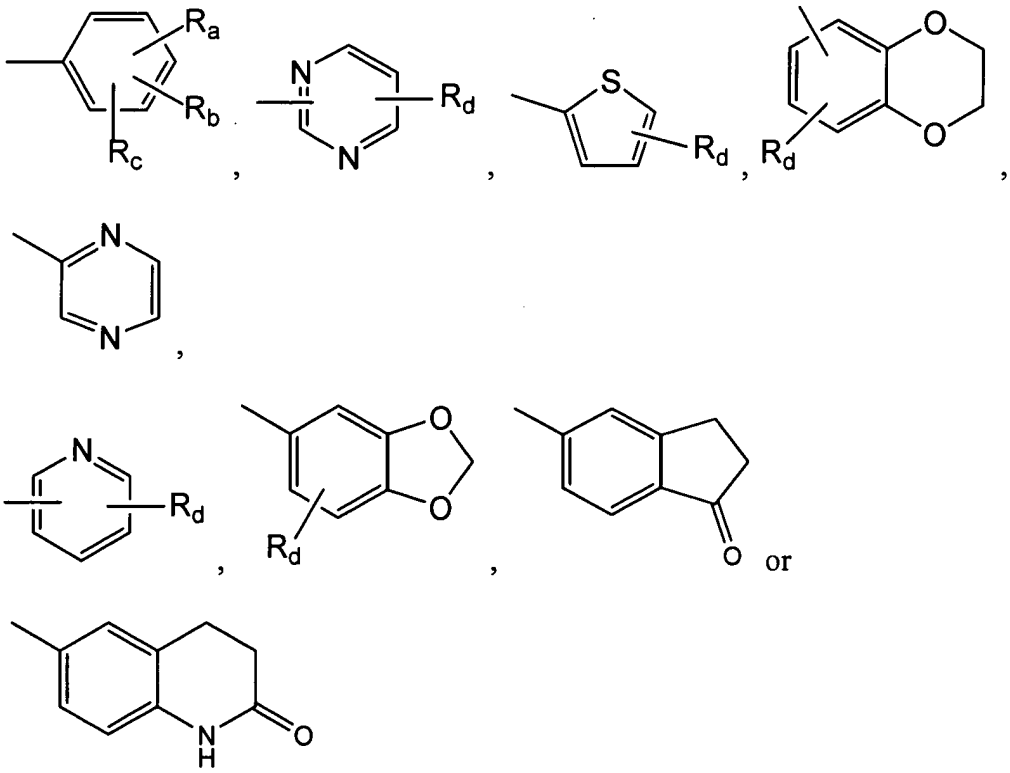
R_1 is hydrogen, (C_{1-4})alkyl, (C_{1-4})alkoxy, hydroxy(C_{1-4})alkyl, cyano, ethynyl, carboxy, (C_{1-4})alkoxycarbonyl, di(C_{1-4})alkylamino, (C_{1-6})alkylaminocarbonyl, or trifluoromethylphenylaminocarbonyl;

R_2 is hydrogen, hydroxy, (C_{1-4}) alkyl, hydroxy (C_{1-4}) alkyl, (C_{1-4}) alkoxy, carboxy, (C_{2-5})alkanoyloxy, (C_{1-4})alkoxycarbonyl, di(C_{1-4})alkylamino(C_{1-4})alkanoyl, di(C_{1-4})alkylaminomethyl, 4-(4-fluorobenzoyl)-piperidin-1-yl-carbonyl, 4-*tert*-butyloxycarbonyl-piperazin-1-yl-carbonyl, 4-(4-azido-2-hydroxybenzoyl)-piperazin-1-yl-carbonyl or 4-(4-azido-2-hydroxy-3-iodobenzoyl)-piperazin-1-yl-carbonyl;

R_3 is hydrogen, (C_{1-4}) alkyl, carboxy, (C_{1-4})alkoxycarbonyl, (C_{1-4})alkylcarbamoyl, hydroxy(C_{1-4})alkyl, di(C_{1-4})alkylaminomethyl, morpholinocarbonyl or 4-(4-fluoro-benzoyl)-piperidin-1-yl-carbonyl;

R_4 is hydrogen, hydroxy, (C_{1-4})alkoxy, carboxy, (C_{2-5})alkanoyloxy, (C_{1-4})alkoxycarbonyl, amino(C_{1-4})alkoxy, di(C_{1-4})alkylamino(C_{1-4})alkoxy, di(C_{1-4})alkylamino(C_{1-4})alkyl, carboxy(C_{1-4})alkylcarbonyl, (C_{1-4})alkoxycarbonyl(C_{1-4})alkoxy, hydroxy(C_{1-4})alkyl, di(C_{1-4})alkylamino(C_{1-4})alkoxy, or m-hydroxy-p-azidophenylcarbonylamino (C_{1-4})alkoxy; and

R_5 is a group of formula



wherein

R_a and R_b independently are hydrogen, hydroxy, halogen, nitro, cyano, carboxy, (C_{1-4})alkyl, (C_{1-4})alkoxy, hydroxy(C_{1-4})alkyl, (C_{1-4})alkoxycarbonyl, (C_{2-7})alkanoyl, (C_{2-5})alkanoyloxy, (C_{2-5})alkanoyloxy(C_{1-4})alkyl, trifluoromethyl, trifluoromethoxy, trimethylsilylethynyl, (C_{2-5})alkynyl, amino, azido, amino(C_{1-4})alkoxy, (C_{2-5})alkanoylamino(C_{1-4})alkoxy, (C_{1-4})alkylamino(C_{1-4})alkoxy, di(C_{1-4})alkylamino(C_{1-4})alkoxy, (C_{1-4})alkylamino,

di(C_{1-4})alkylamino, monohalobenzylamino, thienylmethylamino, thienylcarbonylamino, trifluoromethylphenylaminocarbonyl, tetrazolyl, (C_{2-5})alkanoylamino, benzylcarbonylamino, (C_{1-4})alkylaminocarbonylamino (C_{1-4})alkoxycarbonyl-aminocarbonylamino or (C_{1-4})alkylsulfonyl;

R_c is hydrogen, fluorine, chlorine, bromine, hydroxy, (C_{1-4})alkyl, (C_{2-5})alkanoyloxy, (C_{1-4})alkoxy or cyano; and

R_d is hydrogen, halogen or (C_{1-4})alkyl.

33. (Original) The method of claim 31 wherein said compound has a structure wherein

X_1 is a (C_{2-4})alkenylene, (C_{2-4})haloalkenylene, (C_{2-4})alkynylene or (C_{2-4})haloalkynylene group, wherein each of the foregoing groups is linked via vicinal unsaturated carbon atoms;

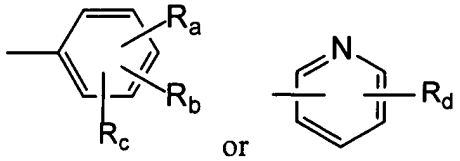
R_1 is hydrogen, (C_{1-4})alkyl, (C_{1-4})alkoxy, cyano, ethynyl or di(C_{1-4})alkylamino;

R_2 is hydrogen, hydroxy, carboxy, (C_{1-4})alkoxycarbonyl, di(C_{1-4})alkylaminomethyl, 4-(4-fluorobenzoyl)-piperidin-1-yl-carbonyl, 4-*tert*-butyloxycarbonyl-piperazin-1-yl-carbonyl, 4-(4-azido-2-hydroxybenzoyl)-piperazin-1-yl-carbonyl or 4-(4-azido-2-hydroxy-3-iodobenzoyl)-piperazin-1-yl-carbonyl;

R_3 is hydrogen, (C_{1-4})alkyl, carboxy, (C_{1-4})alkoxycarbonyl, (C_{1-4})alkylcarbamoyl, hydroxy(C_{1-4})alkyl, di(C_{1-4})alkylaminomethyl, morpholinocarbonyl or 4-(4-fluoro-benzoyl)-piperidin-1-yl-carbonyl;

R_4 is hydrogen, hydroxy, carboxy, (C_{2-5})alkanoyloxy, (C_{1-4})alkoxycarbonyl, amino(C_{1-4})alkoxy, di(C_{1-4})alkylamino(C_{1-4})alkoxy, di(C_{1-4})alkylamino(C_{1-4})alkyl or hydroxy(C_{1-4})alkyl; and

R_5 is a group of formula



wherein

R_a and R_b independently are hydrogen, halogen, nitro, cyano, (C_{1-4})alkyl, (C_{1-4})alkoxy, trifluoromethyl, trifluoromethoxy or (C_{2-5})alkynyl;

R_c is hydrogen, fluorine, chlorine, bromine, hydroxy, (C_{1-4})alkyl, (C_{2-5})alkanoyloxy,

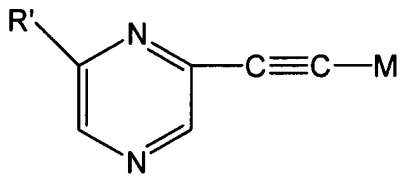
(C_{1-4})alkoxy or cyano; and

R_d is hydrogen, halogen or (C_{1-4})alkyl.

34. (Original) The method of claim 31 wherein said compound is 2-methyl-6-(phenylethynyl)pyridine (MPEP).

35. (Original) The method of claim 31 wherein said compound is 2-methyl-6-(2-phenylethenyl)pyridine (SIB 1893).

36. (Original) The method of claim 1 wherein said compound has a general formula I-A

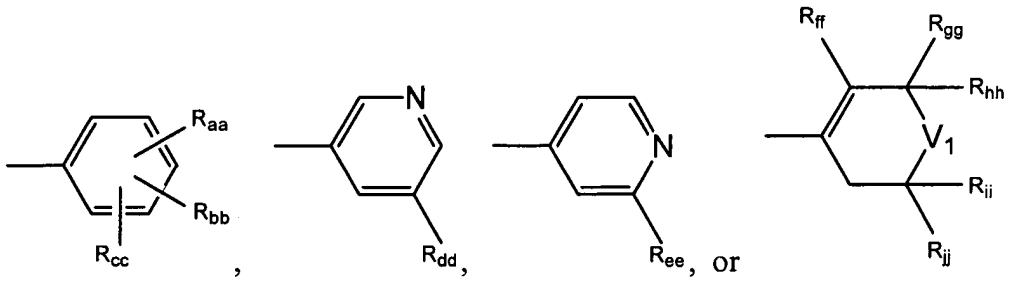


I-A

wherein

R' is hydrogen or (C_{1-4})alkyl and

M is a group of formula



, , , or

wherein

R_{aa}, R_{bb} and R_{cc} are independently of each other hydrogen, (C_{1-4})alkyl, (C_{1-4})alkoxy, hydroxyl, (C_{1-4})hydroxyalkyl, cyano or halo,

R_{dd} is cyano or halo,

R_{ee} is hydroxyl, (C_{1-4})alkyl or (C_{1-4})alkoxy,

R_{ff} is hydrogen or (C_{1-4})alkyl,

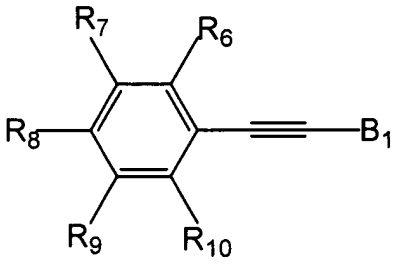
R_{gg} and R_{hh} are hydrogen or together form a group of formula =O, =CH-CN, =N-OH, =N-O-(C_{1-4})alkyl, =CH-$PO_3[(C_{1-4})alkyl]_2$ or =CH-CO-R_{kk}, wherein R_{kk} is (C_{1-4})alkoxy or -$NR_{ll}R_{mm}$, where R_{ll} and R_{mm} are chosen independently from hydrogen, (C_{1-4})alkyl and phenyl,

R_{ii} and R_{jj} are independently hydrogen, (C_{1-4})alkyl or phenyl, and

V_1 is $(CH_2)_n$, CHR_{nn}, wherein n is 1, 2 or 3, R_{nn} is hydroxyl, (C_{1-4})alkyl, (C_{1-4})alkoxy, (C_{1-4})hydroxyalkyl, (C_{1-4})alkoxy(C_{1-4})alkyl, (C_{1-4})alkoxycarbonyl, carbamoyl, (C_{1-4})alkylcarbamoyl, phenyl, pyridyl, thienyl or (R_{oo}, R_{pp})N-lower alkyl, wherein R_{oo} is hydrogen, (C_{1-4})alkyl, (C_{1-4})alkanoyl or benzoyl and R_{pp} is hydrogen or (C_{1-4})alkyl, or, if R_{gg} and R_{hh} are each hydrogen, V_1 can also be NR_{qq}, wherein R_{qq} is (C_{1-4})alkoxycarbonyl, benzyloxycarbonyl, benzoyl, thienyl, (C_{1-4})alkanoyl, carbamoyl, mono- or di-(C_{1-4})-alkylcarbamoyl or phenylcarbamoyl, any phenyl ring in R_{qq} being optionally substituted by one or more halo, cyano, (C_{1-4})alkyl or (C_{1-4})alkoxy groups,

or an enantiomer, diastereoisomer, N-oxide, crystalline form, hydrate, solvate, pharmacologically active metabolite, prodrug, or pharmaceutically acceptable salt thereof.

37. (Original) The method of claim 1 wherein said compound has a general formula II-A

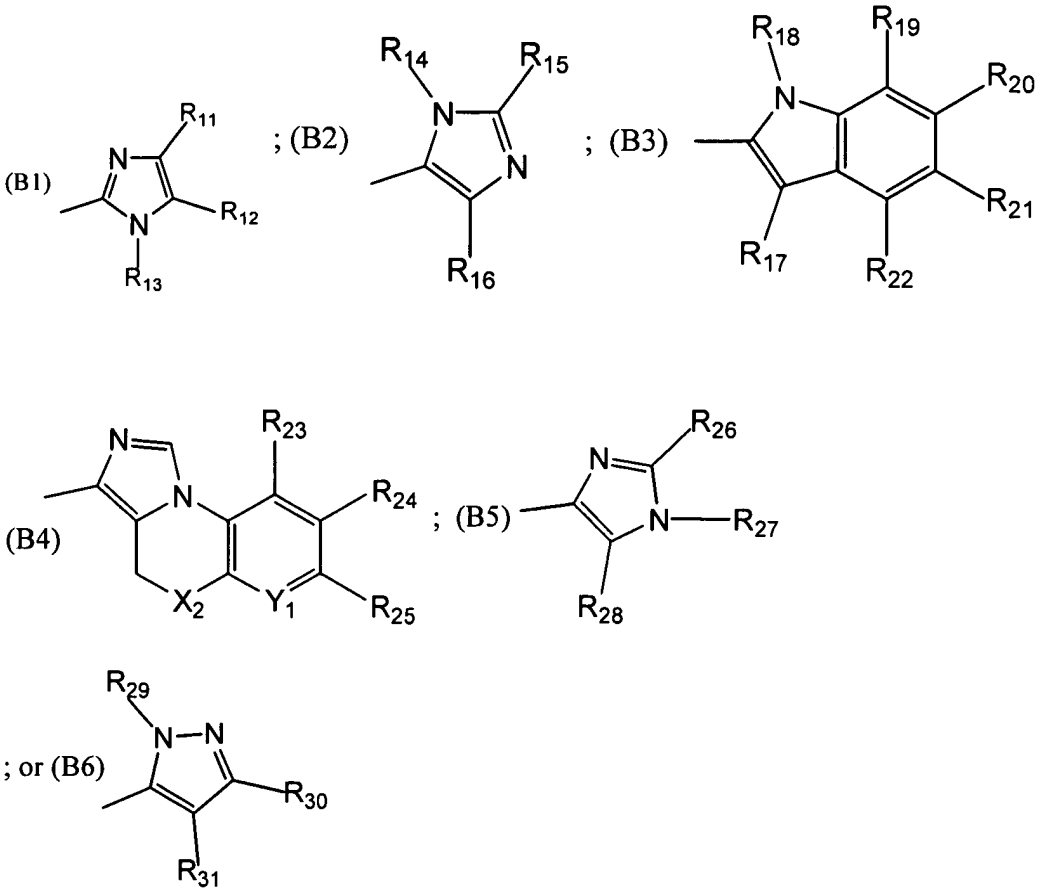


II-A

wherein

R_6, R_7, R_8, R_9 and R_{10} represent, independently from each other, hydrogen, lower alkyl, lower alkoxy, -$(CH_2)_n$-halo, -$(CH_2)_n$-NR_eR_f, -$(CH_2)_n$-$N(R_e)$-C(O)-(lower)alkyl, aryl or heteroaryl, which is unsubstituted or substituted by one or more lower alkyl groups;

B_1 represents



wherein

R_{11} represents hydrogen, lower alkyl, $-(CH_2)_n$-$C(O)OR_e$ or halo;

R_{12} represents hydrogen, lower alkyl, $-(CH_2)_n$-$C(O)OR_f$, halo, nitro or heteroaryl which is unsubstituted or substituted with lower alkyl or cycloalkyl;

R_{13} represents hydrogen, lower alkyl, $-(CH_2)_n$-OH, $-(CH_2)_n$-$C(O)OR_g$ or aryl;

R_{14} represents lower alkyl;

R_{15} represents hydrogen, lower alkyl or halo;

R_{16} represents hydrogen or alkyl;

R_{17} represents $-(CH_2)_n$-$N(R_e)$-C(O)-lower alkyl;

R_{18} represents hydrogen or lower alkyl;

R_{19}, R_{20}, R_{21} and R_{22} represent, independently from each other, hydrogen, lower alkyl, $-(CH_2)_n$-halo or lower alkoxy;

R_{23}, R_{24} and R_{25} represent, independently from each other, hydrogen, lower alkyl, -$(CH_2)_n$-halo or lower alkoxy;

R_{26} represents hydrogen or lower alkyl;

R_{27} represents hydrogen, lower alkyl or lower alkyl substituted with one or more substituents selected from hydroxy and halo;

R_{28} represents hydrogen, lower alkyl, lower alkanoyl or nitro;

R_{29}, R_{30} and R_{31} represent, independently from each other, hydrogen or lower alkyl;

R_e, R_f and R_g represent, independently from each other, hydrogen or lower alkyl;

n is 0, 1, 2, 3, 4, 5 or 6;

X_2 is -CH_2-, -O- or -S-; and

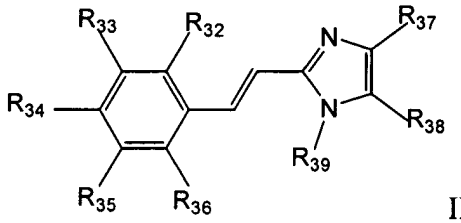
Y_1 is -CH= or -N=;

or an enantiomer, diastereoisomer, N-oxide, crystalline form, hydrate, solvate, pharmacologically active metabolite, prodrug, or pharmaceutically acceptable salt thereof.

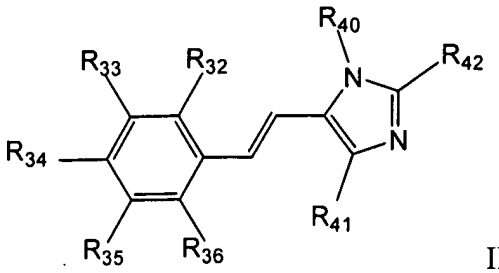
38. (Original) The method of claim 37 wherein B_1 represents B1 and R_{12} represents $(CH_2)_n$-C(O)OR_f, unsubstituted heteroaryl or heteroaryl substituted with one or more lower alkyl or cycloalkyl.

39. (Original) The method of claim 38 wherein R_{12} represents -C(O)O-lower alkyl.

40. (Original) The method of claim 1 wherein said compound has general formula II-B or II-C



II-B



II-C

wherein

R_{32}, R_{33}, R_{34}, R_{35} and R_{36} represent, independently from each other, hydrogen, lower alkyl, -$(CH_2)_n$-halogen, lower alkoxy, -$(CH_2)_n$-NR_eR_f, -$(CH_2)_n$-$N(R_e)$-C(O)-(lower)alkyl, aryl or heteroaryl which is unsubstituted or substituted by one or more lower alkyl residues;

R_{37} represents hydrogen, lower alkyl, -$(CH_2)_n$-$C(O)OR_e$ or halogen;

R_{38} represents hydrogen, lower alkyl, -$(CH_2)_n$-$C(O)OR_f$, halogen, nitro or heteroaryl which is unsubstituted or substituted with lower alkyl or cycloalkyl;

R_{39} represents hydrogen, lower alkyl, -$(CH_2)_n$-OH, -$(CH_2)_n$-$C(O)OR_g$ or aryl;

R_{40} represents lower alkyl;

R_{41} represents hydrogen, halogen or lower alkyl; and

R_{42} represents hydrogen or alkyl;

R_e, R_f and R_g represent, independently from each other, hydrogen or lower alkyl; and

and n = 0, 1, 2, 3, 4, 5, or 6,

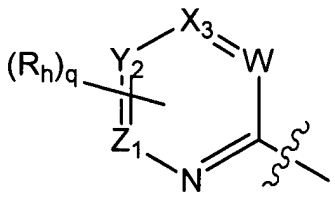
or an enantiomer, diastereoisomer, N-oxide, crystalline form, hydrate, solvate, pharmacologically active metabolite, prodrug, or pharmaceutically acceptable salt thereof.

41. (Currently amended) The method of claim 1 wherein said compound has a general formula III

A_1——L_1—B_2 III

wherein

A_1 is a 5-, 6- or 7-membered ring having the structure



wherein

W, X_3, Y_2 and Z_1 together form a 3-5 membered chain, at least one of W, X_3, Y_2 and Z_1 is a group $(CR_h)_p$, wherein p is 1 or 2; and the remainder of W, X_3, Y_2 and Z_1 are each independently present or absent and when present are each independently C, O, N or S;

each R_h is independently, halogen, substituted or unsubstituted hydrocarbyl, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclic, substituted or unsubstituted lower alkoxy, (lower)alkylcarbonyloxy, carboxyl, esterified carboxyl, amidated carboxyl, substituted or unsubstituted lower alkylthio, substituted or unsubstituted cycloalkyl, mercapto, nitro, carboxyl, carbamate, carboxamide, hydroxyl, ester, cyano, amine, amide, amidine, amido, sulfonyl, sulfonamide or N-(lower)-alkyl-N-phenylcarbamoyl wherein each nitrogen atom is independently unsubstituted or substituted independently with lower alkyl, lower alkoxy, halo or trifluoromethyl and wherein q is 0, 1, 2 or 3;

L_1 is substituted or unsubstituted alkenyl, alkynyl, or azo; and

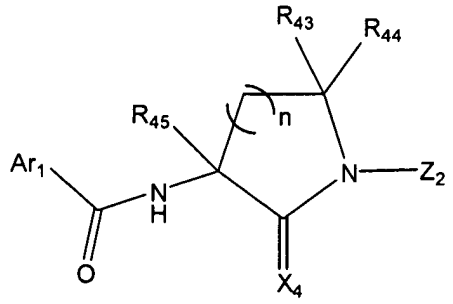
B_2 is substituted or unsubstituted hydrocarbyl, substituted or unsubstituted cyclohydrocarbyl, substituted or unsubstituted heterocyclic, optionally containing one or more double bonds, or substituted or unsubstituted aryl,

wherein "substituted" refers to a radical wherein one or more hydrogen atoms has been replaced with a substituent selected from the group consisting of hydroxyl, alkyl, alkoxy, mercapto, aryl, heterocycle, halogen, trifluoromethyl, pentafluoroethyl, cyano, cyanomethyl, nitro, amino, N-substituted- or N,N-di-substituted amino, wherein one or both nitrogen atoms are substituted ~~independantly~~ independently with alkyl, heterocycle, aryl which are each optionally further substituted ~~independantly~~ independently with hydroxyl, alkyl or heterocycle, or, alkylamide, amidine, amido, carboxy, esterified carboxy, amidated carboxy, carboxamide, carbamate, ester, sulfonyl and sulfonamide groups, and the like,

or an enantiomer, diastereoisomer, N-oxide, crystalline form, hydrate, solvate, pharmacologically active metabolite, prodrug, or pharmaceutically acceptable salt thereof.

42. (Original) The method of claim 41 wherein said administered compound is 3-(2-methylthiazol-4-yl)ethynylpyridine (MTEP).

43. (Original) The method of claim 1 wherein said compound has a general formula IV



IV

wherein,

n is 0, l or 2;

X_4 is O, S, NH, or NOH;

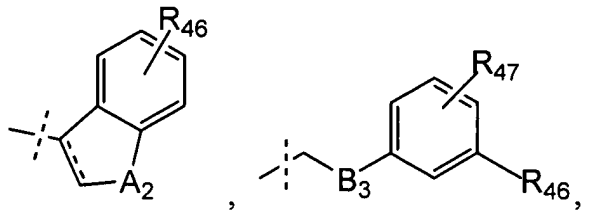
R_{43} and R_{44} are each independently hydrogen, CN, $COOR_i$, $CONHR_i$, (C_{1-6})alkyl, or tetrazole, or R_{43} and R_{44} together represent an oxo group;

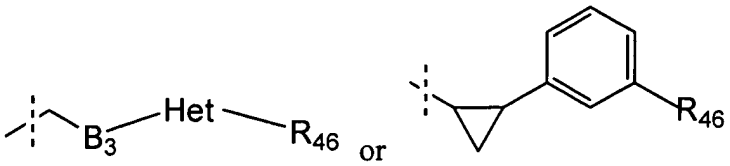
R_i is hydrogen or (C_{1-6})alkyl;

R_{45} is (C_{1-6})alkyl, (C_{2-6})alkenyl, (C_{3-8})cycloalkyl, $-CH_2OH$, $-CH_2O$-alkyl, or -COOH;

Ar_1 is an unsubstituted aromatic or heteroaromatic group or an aromatic or heteroaromatic group substituted with one or more substituent selected from the group consisting of (C_{1-6})alkylamino, di-(C_{1-6})-alkylamino, (C_{1-6})alkoxy, carboxy, hydroxyl, cyano, halo, trifluoromethyl, nitro, amino, (C_{1-6})acylamino, (C_{1-6})alkylthio, (C_{1-6})hydroxyalkyl, (C_{1-6})alkylsulfonyl, and (C_{1-6})haloalkyl;

Z_2 represents a group of the formula





wherein,

R_{46} and R_{47} are each independently from each other hydrogen, halogen, $(C_1\text{-}_6)$alkoxy, -OAr_1, $(C_{1\text{-}6})$alkyl, -CF_3, $COOR_i$, $CONHR_i$, -CN, -OH, COR_i, -S-$(C_{1\text{-}6})$-alkyl, or -SO_2-$(C_{1\text{-}6})$-alkyl;

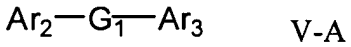
A_2 is CH_2, O, NH, NR_i, S, SO, SO_2, CH_2-CH_2, CH_2O, CHOH, or C(O), where R_i is as defined above;

B_3 is CHR_i, $C(R_i)_2$, $(C_{1\text{-}6})$alkyl, C(O), -CHOH, -CH_2-O, -CH=CH, CH_2-C(O), CH_2-S, CH_2-S(O), CH_2-SO_2, -$CHCO_2R_i$, or -CH-$N(R_i)_2$, where R_i is as defined above; and

Het is a heterocycle,

or an enantiomer, diastereoisomer, N-oxide, crystalline form, hydrate, solvate, pharmacologically active metabolite, prodrug, or pharmaceutically acceptable salt thereof.

44. (Original) The method of claim 1 wherein said compound has general formula V-A



V-A

wherein

Ar_2 is a heteroaryl group,

Ar_3 is an aryl group, where

Ar_2 and Ar_3 are each independently of each other optionally substituted with one or more substituents selected from the group consisting of -F, -Cl, -Br, -I, -OR_j, -SR_j, -SOR_j, -SO_2R_j, -$SO_2NR_jR_k$, -$OCOR_j$, -$OCONR_jR_k$, -$NRCOR_k$, -$NRCO_2R_k$, -CN, -NO_2, -CO_2R_j, -$CONR_jR_k$, -C(O)R_j, - $CH(OR_j)R_k$, -$CH_2(OR_j)$, -R_j, and -A-$(CH_2)_n$-NR_jR_k, wherein R_j and R_k are selected independently from the group consisting of H, CF_3, $(C_1\text{-}_{10})$alkyl, cycloalkyl, alkyl-aryl, alkyl-heteroaryl, heterocycloalkyl, aryl, or R_j and R_k may combine to form a $C_{1\text{-}5}$ methylene chain, and A is defined as CH_2, O, NH, S, SO, SO_2 and n is 1, 2, 3, or 4,

G_1 is selected from the group consisting of -NH-, -S, -O-, -CO-, -CONH-, -$CONHCH_2$-, -CH_2CONH-, -CH_2NHNH-, -$CH_2NHNHCH_2$-, -C=NO-CH_2-, -CH_2NHCH_2-, -CH_2CH_2NH-, -$NHCH_2CO$-, -$NHCH_2CHOH$-, -$NHCH_2NHNH$-, -NHCONH-, or G_1 is a cyclic group selected

from the group consisting of cyclopentane, cyclopentadiene, furan, thiofuran, pyrrolidine, pyrrole, 2-imidazoline, 3-imidazoline, 4-imidazoline, imidazole, pyrazoline, pyrazolidine, imidazolidine, oxazole, 2-oxazole, thiazole, isoxazole, isothiazole, 1*H*-1,2,4-triazole, 1*H*-1,2,3-triazole, 1,2,4-oxathiazole, 1,3,4-oxathiazole, 1,4,2-dioxazole, 1,4,2-oxathiazole, 1,2,4-oxadiazole, 1,2,4-thiadiazole, 1,2,5-oxadiazole, 1,2,5-thiadiazole, 1,3,4-oxadiazole, 1,3,4-thiadiazole, 1*H*-tetrazole, cyclohexane, piperidine, tetrahydropyridine, 1,4-dihydropyridine, pyridine, benzene, tetrahydropyran, 3,4-dihydro-2*H*-pyran, 2*H*-pyran, 4H-pyran, tetrahydrothiopyran, 3,4-dihydro-2*H*-thiopyran, 2*H*-thiin, 4*H*-thiopyran, morpholine, thiomorpholine, piperazine, pyridazine, pyrimidine, pyrazine, 1,2,4-triazine, 1,2,3-triazine, 1,3,5-triazine, and 1,2,4,5-tetrazine groups,

or an enantiomer, diastereoisomer, N-oxide, crystalline form, hydrate, solvate, pharmacologically active metabolite, prodrug, or pharmaceutically acceptable salt thereof.

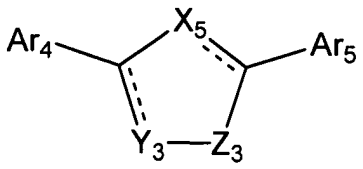
45. (Original) The method of claim 44 wherein Ar_3 is selected from the group consisting of phenyl, benzyl, naphthyl, fluorenyl, anthrenyl, indenyl, phenanthrenyl and benzonaphthenyl groups.

46. (Original) The method of claim 44 wherein Ar_2 is selected from the group consisting of thiazolyl, furyl, pyranyl, 2*H*-pyrrolyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, benzothiazolyl, benzimidazolyl, 3*H*-indolyl, indolyl, indazolyl, purinyl quinolizinyl, isoquinolyl, quinolyl, phthalizinyl, naphthyridinyl, quinazolinyl, cinnolinyl, isothiazolyl, quinoxalinyl, indolizinyl, isoindolyl, benzothienyl, benzofuranyl, isobenzofuranyl and chromenyl groups.

47. (Original) The method of claim 44 wherein Ar_3 is selected from the group consisting of phenyl, benzyl, naphthyl, fluorenyl, anthrenyl, indenyl, phenanthrenyl and benzonaphthenyl groups and Ar_2 is selected from the group consisting of thiazolyl, furyl, pyranyl, 2*H*-pyrrolyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, benzothiazolyl, benzimidazolyl, 3*H*-indolyl, indolyl, indazolyl, purinyl, quinolizinyl, isoquinolyl, quinolyl, phthalizinyl, naphthyridinyl, quinazolinyl, cinnolinyl, isothiazolyl, quinoxalinyl,

indolizinyl, isoindolyl, benzothienyl, benzofuranyl, isobenzofuranyl and chromenyl groups.

48. (Original) The method of claim 1 wherein said compound has a general formula V-B



V-B

wherein

X_5, Y_3, and Z_3 are independently selected from the group consisting of N, O, S, C, and CO wherein at least one of X_5, Y_3, and Z_3 is a heteroatom;

Ar_4 and Ar_5 are independently selected from the group consisting heterocyclic and fused heterocyclic groups containing 1 to 4 heteroatoms selected from the group consisting of N, O, and S and an aromatic group selected from the group consisting of phenyl, benzyl, 1-naphthyl, 2-naphthyl, fluorenyl, anthrenyl, indenyl, phenanthrenyl, and benzonaphthenyl, wherein Ar_4 and Ar_5 are optionally substituted with one or more substituents selected from the group consisting of -F, -Cl, -Br, -I, $-OR_j$, $-SR_j$, $-SOR_j$, $-SO_2R_j$, $-SO_2NR_jR_k$, $-OCOR_j$, $-OCONR_jR_k$, $-NRCOR_k$, $-NRCO_2R_k$, -CN, $-NO_2$, $-CO_2R_j$, $-CONR_jR_k$, $-C(O)R_j$, $-CH(OR_j)R_k$, $-CH_2(OR_j)-R_j$, and $-A-(CH_2)_n-NR_jR_k$; wherein R_j and R_k are selected independently from the group consisting of H, CF_3, (C_{1-10})alkyl, cycloalkyl, alkyl-aryl, alkyl-heteroaryl, heterocycloalkyl, aryl, or R_j and R_k may combine to form a C_{1-5} methylene chain, A is defined as CH_2, O, NH, S, SO, SO_2,

and n is 1, 2, 3, or 4,

or an enantiomer, diastereoisomer, N-oxide, crystalline form, hydrate, solvate, pharmacologically active metabolite, prodrug, or pharmaceutically acceptable salt thereof.

49. (Original) The method of claim 48 wherein said heterocyclic or fused heterocylic group is selected from the group consisting of quinolyl, quinazolyl, quinoxalyl, 2-pyrimidyl, 4-pyrimidyl, 5-pyrimidyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, and pyrazyl.

50. (Original) A method of identifying a compound useful for treating neuromuscular dysfunction of the lower urinary tract in a mammal, comprising

(a) determining the binding affinities of one or more test compound for an mGlu5 receptor and one or more of an mGlu1 receptor or Group II mGlu receptor;

(b) identifying a test compound that

(1) binds to mGlu5 receptor with an affinity of at least 10^{-6} M; and

(2) binds to mGlu5 receptor with an affinity at least 10-fold stronger than the affinity for mGlu1 receptor or Group II mGlu receptor.

51. (Original) The method of claim 50 further comprising

individually measuring the binding affinity of said one or more test compounds for one or more Group III mGlu receptor and

identifying a test compound that binds to mGlu5 receptor with an affinity at least 10-fold stronger than the affinity for a Group III mGlu receptor.

52. (Original) The method of claim 50 or 51 wherein step (b) comprises identifying a test compounds that

(1) binds to mGlu5 receptor with an affinity of at least 10^{-6} M; and

(2) binds to mGlu5 receptor with an affinity at least 10-fold stronger than the affinity for each of mGlu1 receptor and Group II mGlu receptor.

53. (Original) The method of claim 50 or 51 wherein step (b) comprises identifying a test compounds that

(1) binds to mGlu5 receptor with an affinity of at least 10^{-6} M; and

(2) binds to mGlu5 receptor with an affinity at least 100-fold stronger than the affinity for a mGlu1 receptor or Group II mGlu receptor.

54. (Original) The method of claim 53 wherein step (b) comprises identifying a test compounds that

(1) binds to mGlu5 receptor with an affinity of at least 10^{-6} M; and

(2) binds to mGlu5 receptor with an affinity at least 100-fold stronger than the affinity for each of mGlu1 receptor and Group II mGlu receptor.

55. (Original) The method of claim 50 or 51 further comprising measuring the ability of each of said identified test compound to act as an antagonist or inverse agonist at the mGlu5 receptor.

56. (Original) The method of claim 50 or 51 wherein said neuromuscular dysfunction is urinary urgency, overactive bladder, increased urinary frequency, decreased urinary compliance, cystitis, incontinence, urine leakage, enuresis, dysuria, urinary hesitancy or difficulty in emptying the bladder.

57. (Original) The method of claim 56 wherein said neuromuscular dysfunction that is decreased urinary compliance is decreased bladder storage capacity.

58. (Original) The method of claim 56 wherein said neuromuscular dysfunction that is cystitis is interstitial cystitis.